PATENT COOPERATION TREATY

PCT/JP2007/063946

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)

(PCT Rules 44*bis*.3(c) and 72.2)

To:

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JAPON

Date of mailing *(day/month/year)*	
29 January 2009 (29.01.2009)	
Applicant's or agent's file reference C1-A0604P	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2007/063946	International filing date *(day/month/year)* 13 July 2007 (13.07.2007)
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

EP

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

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Authorized officer

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference C1-A0604P	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2007/063946	International filing date *(day/month/year)* 13 July 2007 (13.07.2007)	Priority date *(day/month/year)* 13 July 2006 (13.07.2006)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 20 January 2009 (20.01.2009)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara e-mail: pt07.pct@wipo.int

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference C1-A0604P	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2007/063946	13.07.2007	13.07.2006

International Patent Classification (IPC) or both national classification and IPC

Applicant
CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2007/063946

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ *the international application in the language in which it was filed*

☐ the translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rule 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☒ in electronic form

c. time of filing/furnishing

☒ contained in the international application as filed

☐ filed together with the international application in electronic form

☐ furnished subsequently to this Authority for the purposes of search

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2007/063946

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 8

because:

☐ the said international application, or the said claims Nos. ______ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 8 are so unclear that no meaningful opinion could be formed (*specify*):

Claim 8 specifies an antibody with a function of "binding to an epitope the same as that of a human leukocyte antigen (HLA) protein to which the antibody in any one of claims 1-7 binds", but no epitope recognized by the antibody in the invention of this application is specified in the description of this application, and therefore claim 8 is quite obscure because it is not clear what antibody is encompassed.

☐ the claims, or said claims Nos. ______ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 8

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/JP2007/063946

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-7, 9-25	YES
	Claims		NO
Inventive step (IS)	Claims	1-7, 9-25	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-7, 9-25	YES
	Claims		NO

2. Citations and explanations:

Document 1: WO 2004/033499 A1 (Chugai Pharmaceutical Co., Ltd.), 22 April 2004, full text & EP 1561759 A1

Document 2: Kimura N. et al., 2D7 diabody bound to the alpha2 domain of HLA class I efficiently induces caspase-independent cell death against malignant and activated lymphoid cells, Biochem. Biophys. Res. Commun., 2004, Vol. 325, No. 4, pages 1201 to 1209, abstract

Document 3: Genestier L. et al., Fas-independent apoptosis of activated T cells induced by antibodies to the HLA class I alpha1 domain, Blood, 1997, Vol. 90, No. 9, pages 3629 to 3639, abstract

Concerning claims 1-7 and 9-23

The invention as set forth in claims 1-7 and 9-23 is novel and involves an inventive step in view of documents 1-3 cited in the ISR.

Documents 1 and 2 describe that a monoclonal antibody to the α2 domain of HLA was obtained, that a low-molecular antibody was fabricated using a variable region of said antibody and that the low-molecular antibody is cytotoxic.

Document 3 describes that an antibody to the α2 domain of HLA was obtained and that said antibody inhibits cell

proliferation but does not cause apoptosis.

The antibody of the invention of this application is an antibody which specifically recognizes the α2 domain of HLA, but there is no technique wherein CDRs 1, 2 and 3 of a heavy chain variable region of the anti-HLA α2 domain antibody are identified with SEQ ID NOs: 7, 8 and 9, respectively, and CDRs 1, 2 and 3 of a light chain variable region are identified with SEQ ID NOs: 10, 11 and 12, respectively, and said antibody is a novel protein. Furthermore, it is apparent that the low-molecular antibody of the invention of this application has an excellent cell proliferation inhibiting capability as compared to the antibodies described in documents 1-3.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2007/063946

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

In the antibody in claims 1 and 3, the positions of CDR in the heavy chain variable region to which SEQ ID NOs: 7, 8 and 9 correspond are not adequately identified, and CDR1=SEQ ID NO: 7, CDR2=SEQ ID NO: 8 and CDR3=SEQ ID NO: 9 are merely mentioned in the description of the present application, and so the feature of the invention as in claims 1 and 3 is not considered to be set forth adequately in the description.

In the antibody in claims 2 and 3, the positions of CDR in the light chain variable region to which SEQ ID NOs: 10, 11 and 12 correspond are not adequately identified, and CDR1=SEQ ID NO: 10, CDR2=SEQ ID NO: 11 and CDR3=SEQ ID NO: 12 are merely mentioned in the description of the present application, and so the feature of the invention as in claims 2 and 3 is not considered to be set forth adequately in the description.

Concerning the antibody having "amino acid sequences with one or more amino acid sequences replaced, lost, inserted and/or added" in claims 4-7 (b) and (f), SEQ ID NOs: 2, 4 and 6 each include a CDR region, and if amino acid residues are "replaced, lost, inserted and/or added" in said region, the activity of said antibody is likely reduced, and whether a desired effect is exhibited is unclear.

Claim 25 claims "an autoimmune disease therapeutic agent containing as an effective ingredient the antibody set forth in any of claims 1-14", but it is not described that the disease could be actually treated using the antibody of the invention of this application, and so the feature of the

Box No. VIII Certain observations on the international application

invention as in claim 25 is not considered to be set forth adequately in the description.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2007/063946

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC)

C12N15/00(2006.01)i, A61K39/395(2006.01)i,
A61P7/00(2006.01)i, A61P35/00(2006.01)i,
C07K16/18(2006.01)i, C12N1/15(2006.01)i,
C12N1/19(2006.01)i, C12N1/21(2006.01)i,
C12N5/10(2006.01)i, C12N15/09(2006.01)i,
C12P21/08(2006.01)i